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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/647,268	08/20/2003	Teruko Osumi	0155.02	2068

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USDA-ARS-OFFICE OF TECHNOLOGY TRANSFER
PATENT ADVISORS OFFICE
WESTERN REGIONAL RESEARCH CENTER
800 BUCHANAN ST
ALBANY, CA 94710

EXAMINER	
IBRAHIM, MEDINA AHMED	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 05/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/647,268	OSUMI ET AL.	
	Examiner	Art Unit	
	Medina A. Ibrahim	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-9 and 11-15* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-9 and 11-15, in the reply filed on 03/10/05 is acknowledged. The restriction requirement is made FINAL.

Claims 1-15 are pending.

Claim 10 has been withdrawn from consideration as being directed to a non-elected invention.

Claims 1-9 and 11-15 are under consideration.

Sequence Listing

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and amino acid sequences set forth in 37 CFR1.821 (a)(1) and (a) (2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. The CRF and paper sequence listing filed of July 2004 have been entered. However, the sequences of Figures 6-7 have not been identified by SEQ ID NO: in the Brief Description of the Drawings on page 8 of the specification. Applicant is respectfully requested to identify the sequence presented in the figures or to submit a new Sequence Listing which comprises said sequence. Applicant is also required to amend the specification, page 8, to insert said SEQ ID Nos.

Specification

The disclosure is objected to because of the following informalities: for example, pages 11 and 12, paragraphs 0046 and 0047, contain embedded hyperlinks directed to an Internet address. The use of hyperlinks and/or other form of browser- executable

code are not permitted under USPTO current policy because the content of such links are subject to a change, resulting in the introduction of New Matter into the specification. Applicant is required to delete the embedded hyperlink and/or other form of browser- executable code. See MPEP 608.01.

Claim Objections

At claim 1, parts (b) and (c), "sequence" should be replaced with ---molecule-- to be consistent with the parts (a) and (d) of the Markush group.

At claims 3, " a nucleic acid molecule" should be changed to --the nucleic acid molecule--- because it refers to a previous claim.

At claims 15, " a nucleic acid molecule" in lines 2-3 should be changed to --the nucleic acid molecule--- because it refers to a previous claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-9 and 11-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite for failing to recite the specific hybridization and wash conditions (salt concentration, temperature, time) required for Applicant's "high stringent" conditions. Hybridization conditions vary from one laboratory to another, and

what is high stringency for one may be high stringency for another. The specification fails to define the appropriate wash/hybridization conditions, and hence, what is encompassed by the claim is unclear. Appropriate correction is required to more clearly define the metes and bounds of the claim. Dependent claims 3-9 and 11-15 are included in the rejection.

Claim 9 is indefinite in the recitation of "sexually or asexually derived progeny" because what the derived progeny encompasses is unclear. Since "progeny" will encompass progeny plants produced by any means, it is suggested that "Sexually or asexually derived progeny" be replaced with ---A progeny---.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 6 and 9 are rejected under 35 U.S.C. 101 because the claimed invention is directed to a non-statutory subject matter. The claims do not read, "transgenic" seed or progeny, or "wherein the seed/progeny comprises the nucleic acid molecule". Due to chimerism, not all of the cells/tissues/organs from a transgenic plant will comprise in their genome the transgene. Given that there is no indication that there would be any other distinguishable characteristics of the claimed seed/progeny, it is unclear whether the claimed seed/cell would be distinguishable from seed/progeny that would occur in nature. See *Diamond v. Chakrabarty* 447 U.S. 303 (1980, Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 76 USPQ 280 (1948), and In re Bergy, Coats, and Malik

195 USPQ 344, (CCPA) 1977. An Amendment to the claims to insert ----transgenic--- before, "A" in claim 6, and before "progeny" in claim 9 would obviate the rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-9 and 11-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the isolated nucleic acid molecule encoding SEQ ID NO: 2, 4, or 10, a plant/cell/seed/progeny transformed with said nucleic acid molecule, and a method for conferring resistance against Solanum bulbocastanum late blight disease, does not reasonably provide enablement for a nucleic acid molecule having more than 93% sequence identity to SEQ ID NO: 1 from nucleotides 52 to 3018 and a hybridizing sequence thereof, a nucleic acid molecule encoding a polypeptide having more than 90% sequence identity to SEQ ID NO: 2, 4, or 10, and a method that employs said nucleic acid molecules for production of fungal resistant transgenic plants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use of the invention commensurate in scope with these claims.

The claims are broadly drawn to a nucleic acid molecule having a coding sequence that is more than 93% identical to SEQ ID NO: 1 from nucleotides 51 to 3018,

a nucleic acid sequence that hybridizes thereto under high stringency conditions, said nucleic acid molecules encoding a plant disease resistance polypeptide, and nucleic acid molecule which encodes a polypeptide having more than 90% sequence identity to SEQ ID NO: 2, 4, or 10 and having disease resistance activity. The claims are also drawn to a nucleic acid construct comprising said nucleic acid molecule, plant/cell transformed with said nucleic acid molecule, and a method of conferring or enhancing a plant's resistance to fungal diseases by transforming the plant with said nucleic acid molecule.

Applicant teaches map-based cloning and identification of the S. bulbocastanum late blight resistance genes designated as Sbul from potatoes (FIG. 2). Applicant also teaches a cDNA sequence (SEQ ID N0: 1 encoding SEQ ID N0: 2), and the genomic DNA containing a 412 bp intron shown in SEQ ID N0: 3 encoding SEQ ID N0: 4. Applicant further teaches that the polypeptides encoded by Sbu1 genes are disease resistant polypeptides as they have similarities with other known NBS- LRR polypeptides (Fig. 3). Applicant also teaches a genomic chimeric transgene comprising the Sbul1 DNA operably linked to the potato Ubi3 promoter in a vector (Fig. 4), and transformation of susceptible potato plant/cells with said vector. Applicant also teaches screening of the transgenic potato plants for resistance against *P. infestans* by detached leaf assay. Results show that both the Sbull genomic and CDNA transgenes conferred resistance to P. infestans in transgenic potatoes (FIG. 5), while other Sbu1 genes (Sbu12 and Sbu13) having sequence identity of 93% in the coding region (Fig. 7) didn't confer resistance when individually expressed in transgenic potato plants (Fig. 6).

In re Wands (858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988) lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

Applicant has not provided guidance for the obtention and use of nucleic acid molecules having more than 90% sequence identity to SEQ ID NO: 1 from nucleotides 52 to 3018 and nucleic acids that hybridize thereto under unspecified hybridization conditions and encoding a disease resistance polypeptide. Applicant has not taught how and where to modify the full-length sequences of SEQ ID NO: 1 or 2, 4, and 10 in order to obtain sequences having both the structural and functional properties as recited in the claims. Therefore, Applicant has not provided guidance for a representative number of nucleic acids having the structural and functional properties as recited in the claims. In the working examples, Applicant discloses nucleic acid sequences (Sbu12 and Sub13) having 93% sequence identity with SEQ ID NO: 1 from nucleotide 52 to nucleotide 3018 that didn't encode a functional disease resistance polypeptide when expressed in potato plants (paragraph 0059). To claim nucleic acid sequences from any source having more than 93% to SEQ ID NO: 1 from nucleotide 52 to nucleotide 3018, hybridizing sequences thereof, nucleic acid sequences encoding polypeptides having more than 90% sequence identity to SEQ ID NO: 2, 4, or 10 is an invitation to

experiment as to whether the nucleic acid sequences having such structural property would confer resistance to diseases which would require undue and excessive experimentation.

Parker et al (The Plant Cell (1996), vol. 8, pp. 2033-2046) teach that despite the insights that resistance genes have LRR and/or NBS, the function of these genes cannot be predicted from sequence structure alone and functional tests are required to determine their role in resistance (see the whole document, especially page 2042, column 1, last full paragraph).

The state of the art for isolation of cDNA or genomic clones with specific function is highly unpredictable. Significant guidance is required with respect to hybridization and wash (or PCR) conditions; probe (or primer) sequences that will allow specific isolation of the target genes from all plant sources. In the absence of specific guidance, undue trial and error experimentation would be required to screen through the vast number of nucleic acid sequence having more than 93% sequence identity to SEQ ID NO: 1 or that would hybridize thereto identify those that encode a functional polypeptide that induce resistance against *all diseases* and that also affects the disease resistance activity in a transgenic plant. Undue experimentation would also be required to screen through the vast number of nucleic acid sequences encoding polypeptides having more than 90% sequence identity to SEQ ID NO: 2, 4, or 10, to determine those that retain the desired functional activity when expressing a transgenic plant.

Furthermore, since the working example disclosed in the specification is limited to the use of the nucleic acid molecule of SEQ ID NO: 1, 3 or 9, the ability of SEQ ID

NO: 1, 3, or 9 to confer resistance against P. infestans cannot be extrapolated to all other diseases and to all nucleic acids having more than 93% sequence identity to SEQ ID NO: 1 and nucleic acids that hybridize thereto under high stringency conditions and nucleic acid sequences encoding polypeptides having more than 90% sequence identity to SEQ ID NO: 2, 4, or 10, absent specific guidance.

When In re Wands factors are weighed it is concluded that undue experimentation would be required to practice the invention throughout the full scope of the claims, and therefore the invention is not enabled.

Written Description

Claims 1, 3-9 and 11-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of nucleic acid molecules having a coding sequence that is more than 93% identical to SEQ ID NO: 1 from nucleotides 51 to 3018, nucleic acid sequences that hybridize thereto under high stringency conditions and encoding a plant disease resistance polypeptide, and nucleic acid molecules which encodes a polypeptide having more than 90% sequence identity to SEQ ID NO: 2, 4, or 10 and having disease resistance activity. The claims are also drawn to nucleic acid constructs comprising said nucleic acid molecules, plants/cells transformed with said nucleic acid molecules, and a method of conferring or enhancing a plant's resistance to

fungal diseases by transforming the plant with said nucleic acid molecule. In contrast, Applicant describes a nucleic acid molecule encoding SEQ ID NO: 2, 4 or 10. Applicant also describes a nucleic acid construct comprising said nucleic acid molecule, plant/ cell transformed with said nucleic acid molecule, and a method of transforming plants with said nucleic acid molecule for resistance against P. infestans. These are genus claims.

In *Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), the court stated:

> An adequate written description of a DNA "requires a precise definition, such as by structure, formula, chemical name, or physical properties", not a mere wish or plan for obtaining the claimed chemical invention... Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it; what is required is a description of the DNA itself (43 USPQ2d at 1404).

The court held that held that human insulin-encoding cDNA is not described by prophetic example, which sets forth only a general method for obtaining the human cDNA:

> The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity...Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes...does not necessarily describe the DNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA....Accordingly, the specification does not provide a written description of human cDNA (43 USPQ2d at 1405).

The description of a single species of rat cDNA was held insufficient to describe the broad genera of vertebrate or mammalian insulin:

> "In claims to genetic material...a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It doesn't define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function...does not suffice to define the genus

because it is only an indication of what the gene does, rather than what it is (43 USPQ2d at 1406).

The court continued:

"Thus...a cDNA is not defined by the mere name 'cDNA', even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA...A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus". (43 USPQ2d at 1406). See, also where the court teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from the organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

Applicant has not described the composition or structure of all the nucleotide as broadly claimed. A substantial variation in structures and function is expected among nucleic acid sequences that hybridize to SEQ ID NO: 1 from nucleotide 52 to nucleotide 3018 under unspecified high stringency conditions. Nucleic acid sequences from any source having more than 93% sequence identity to SEQ ID NO: 1 are not expected to confer disease resistance because the nucleic acid sequences (Sbu12 and Sbu13) from potato having 93% sequence identity in the coding region didn't confer resistance to P. infestans when expressed in susceptible potato plants. Therefore, Applicant has not described a representative number of nucleotide sequences of the genus of the claims. In addition, since Applicants has not described the nucleic acids of the claims as discussed above, nucleic acid constructs, cells and plants cell comprising said nucleic acids, and the use of said nucleic acids are similarly not described. See Written description Examination Guidelines published in Federal Registry/Vol. 66, No.4/Friday,

January 5, 2001/Notices).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

((b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-9 and 11-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Fluhr et al (US 6, 100, 449).

The claims are drawn an isolated nucleic acid molecule that hybridizes to SEQ ID NO: 1 from nucleotide position 52 to nucleotide position 3018 under high stringency conditions and encoding a disease polypeptide, a nucleic acid construct comprising it, plant cell, plant/seed transformed with said nucleic acid molecule, progeny of said plant, and a method for producing a disease resistance polypeptide, and a method for conferring resistance against fungal late blight diseases. The specification does not clearly define what is encompassed by the high stringency conditions.

Fluhr et al teach an isolated gene from Fusarium resistance locus in tomato encoding disease resistance polypeptides comprising LRR regions (columns 2 and 6, last full paragraph; Example 5). Fluhr et al also teach a vector comprising said gene, transformation of plants; transformed plants/cell/seed/progeny including members of the Solanaceae family such as tomato and parts thereof transformed with said vector, and a method of expressing and producing resistance polypeptide in a plant cell (column 2-8

and Examples 6-7; and columns 77-80). Resistance to phytophthora infestans and other fungi would be inherent property of the transgenic plant expressing LRR containing resistant polypeptides. Also there is no known difficulty of transforming potato plants for disease resistance. Given the broad interpretation of high stringency conditions, the claimed nucleic acid molecules would encompass the gene disclosed by the cited reference, absent evidence to the contrary. Therefore, Fluhr et al teach all claim limitations.

Remarks

Claim 2 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No claim is allowed.

Contact information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Medina A. Ibrahim whose telephone number is (571) 272-0797. The Examiner can normally be reached Monday -Thursday from 8:00AM to 5:30PM and every other Friday from 9:00AM to 5:00 PM. Before and after final responses should be directed to fax nos. (703) 872-9306 and (703) 872-9307, respectively.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Amy Nelson, can be reached at (571) 272-0804.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you

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MEDINA A. IBRAHIM
PATENT EXAMINER